

CLAIMS

WE CLAIM:

1. A method for elongating polymeric molecules comprising the steps of:
 - (a) passing a liquid and polymeric molecule through a micro-channel sized to provide laminar flow of the liquid along a micro-channel length; and
 - (b) controlling the flow of liquid to cause elongation of the polymeric molecule within the laminar flow.
2. The elongation method of claim 1 wherein the micro-channel has a cross-sectional dimension within one order of magnitude of a relaxed diameter of the polymeric molecule.
3. The elongation method of claim 1 wherein the micro-channel includes a transparent wall and including the step of optically analyzing the elongated polymeric molecule suspended within the laminar flow.
4. The elongation method of claim 1 including the step of reacting the elongated polymeric molecule suspended within the laminar flow with a reactant.
5. The elongation method of claim 4 wherein the reactant is an enzyme causing cleavage of the polymeric molecule.
6. The elongation method of claim 4 wherein the reactant is a second polymeric molecule reacting with at least one elongated polymeric molecule.
7. The elongation method of claim 6 wherein the polymeric molecules are DNA.
8. The elongation method of claim 1 wherein multiple polymeric molecules are simultaneously passed through the channel.
9. The elongation method of claim 1 including the step of staging the polymeric molecule with a plurality of other polymeric molecules in the liquid before passage through the channel.

10. The elongation method of claim 1 including the step of periodically reversing the flow to cause the polymeric molecule to hover in an elongated state.

11. The elongation method of claim 10 wherein the flow is periodically reversed at a rate from between 0.2-5 Hz.

12. The elongation method of claim 10 wherein the micro-channel includes a transparent wall and including the step of optically analyzing the elongated polymeric molecule as it hovers within the laminar flow.

13. The elongation method of claim 10 including the step of reacting the elongated polymeric molecule hovering within the laminar flow with a reactant.

14. The elongation method of claim 13 wherein the reactant is an enzyme causing cleavage of the polymeric molecule.

15. The elongation method of claim 13 wherein the reactant is a second polymeric molecule.

16. The elongation method of claim 15 wherein the polymeric molecules are DNA.

17. The elongation method of claim 1 wherein at least a first wall of the micro-channel provides attraction to the polymeric molecule and further including the step of:

(c) adsorbing of the polymeric molecule to the first wall of the micro-channel in straightened form.

18. The elongation method of claim 17 wherein step (c) includes the steps of controlling the flow rate of the liquid and the size of the micro-channel to cause adsorption by random encounters between at least one end of the polymeric molecule and a wall of the micro-channel.

19. The elongation method of claim 17 wherein step (c) includes the step of applying an acceleration across the width of the micro-channel to cause adsorption of the polymeric molecule to one wall of the micro-channel.

20. The elongation method of claim 17 wherein step (c) includes the step of applying an electrostatic field across the width of the micro-channel to cause adsorption of the polymeric molecule to one wall of the micro-channel.

21. The elongation method of claim 17 wherein the micro-channel includes an elastic channel material releasably adhered to an optical mapping surface to create the micro-channel between the elastic material and the optical mapping surface;

and wherein the adsorption is to the optical mapping surface.

22. The elongation method of claim 21 further including the step of separating the elastic channel material from the optical mapping surface after adsorption of the polymeric molecule to the optical mapping surface.

23. The elongation method of claim 17 further including the step of reacting the adsorbed polymeric molecule with a reactant.

24. The elongation method of claim 23 wherein the reactant is an enzyme causing cleavage of the polymeric molecule.

25. A method for aligning polymeric molecules comprising the steps of:

(a) passing a liquid and a plurality of polymeric molecules through a micro-channel sized to provide laminar flow of the liquid along a micro-channel length; and

(b) controlling the flow of liquid to cause alignment of the polymeric molecules within the laminar flow.

26. The alignment method of claim 25 wherein the micro-channel has a cross-sectional dimension within one order of magnitude of a relaxed diameter of the longest polymeric molecule.

27. The alignment method of claim 25 wherein the micro-channel includes a transparent wall and including the step of optically analyzing the aligned polymeric molecules suspended within the laminar flow.

28. The alignment method of claim 25 including the step of reacting the aligned polymeric molecules suspended within the laminar flow with a reactant.

29. The alignment method of claim 28 wherein the reactant is an enzyme causing cleavage of the polymeric molecules.

30. The alignment method of claim 28 wherein the reactant is a second polymeric molecule reacting with at least one aligned polymeric molecule.

31. The alignment method of claim 25 wherein the polymeric molecules are DNA.

32. The alignment method of claim 25 including the step of periodically reversing the flow to cause the polymeric molecules to hover in an aligned state.

33. The alignment method of claim 32 wherein the flow is periodically reversed at a rate from between 0.2-5 Hz.

34. The elongation method of claim 32 wherein the micro-channel includes a transparent wall and including the step of optically analyzing the aligned polymeric molecules as they hover within the laminar flow.

35. The elongation method of claim 32 including the step of reacting the aligned polymeric molecules hovering within the laminar flow with a reactant.

36. The alignment method of claim 35 wherein the reactant is an enzyme causing cleavage of the polymeric molecules.

37. The alignment method of claim 35 wherein the reactant is a second polymeric molecule.

38. The alignment method of claim 35 wherein the polymeric molecules are DNA.

39. The alignment method of claim 25 wherein at least a first wall of the micro-channel provides attraction to the polymeric molecules and further including the step of:

(c) adsorbing of the polymeric molecules to the first wall of the micro-channel in aligned form.

40. The alignment method of claim 39 wherein step (c) includes the steps of controlling the flow rate of the liquid and the size of the micro-channel to cause adsorption by random encounters between at least one end of the polymeric molecules and a wall of the micro-channel.

41. The alignment method of claim 39 wherein step (c) includes the step of applying an acceleration across the width of the micro-channel to cause adsorption of the polymeric molecules to one wall of the micro-channel.

42. The alignment method of claim 39 wherein step (c) includes the step of applying an electrostatic field across the width of the micro-channel to cause adsorption of the polymeric molecules to one wall of the micro-channel.

43. The alignment method of claim 39 wherein the micro-channel includes an elastic channel material releasably adhered to an optical mapping surface to create the micro-channel between the elastic material and the optical mapping surface;

and wherein the adsorption is to the optical mapping surface.

44. The alignment method of claim 43 further including the step of separating the elastic channel material from the optical mapping surface after adsorption of the polymeric molecules to the optical mapping surface.

45. The alignment method of claim 39 further including the step of reacting the adsorbed polymeric molecules with a reactant.

46. The elongation method of claim 45 wherein the reactant is an enzyme causing cleavage of the polymeric molecules.

47. The elongation method of claim 25 wherein the micro-channel includes a transparent wall and including the step of optically analyzing the aligned polymeric molecules within the laminar flow.

48. A method for separating polymeric molecules of differing molecular weight comprising the steps of:

- (a) passing a liquid and polymeric molecules through a micro-channel sized to provide laminar flow of the liquid along a micro-channel length; and
- (b) controlling the laminar flow of liquid to separate the polymeric molecules of differing molecular weights.

49. The separation method of claim 48 further including the step of controlling the flow of liquid to elongate the molecules and separate the elongated molecules by their relative speeds within the laminar flow.

50. The separation method of claim 49 further including the step of periodically reversing the laminar flow to cause the polymeric molecules to hover in an elongated state after separation.

51. The separation method of claim 50 wherein the flow is periodically reversed at a rate from between 0.2-5 Hz.

52. The separation method of claim 50 wherein the micro-channel includes a transparent wall and including the step of optically analyzing the separated polymeric molecules as they hover within the laminar flow.

53. The separation method of claim 50 including the step of reacting the separated polymeric molecules hovering within the laminar flow with a reactant.

54. The separation method of claim 53 wherein the reactant is an enzyme causing cleavage of at least one polymeric molecule.

55. The separation method of claim 53 wherein the reactant is a second polymeric molecule.

56. The separation method of claim 55 wherein the polymeric molecules are DNA.

57. The separation method of claim 49 further including the step of fixing the separated polymeric molecules to a substrate after their separation.

58. The separation method of claim 57 wherein the micro-channel includes an elastic channel material releasably adhered to an optical mapping surface to create the micro-channel between the elastic material and the optical mapping surface;

and separated polymeric molecules are fixed to the optical mapping surface.

59. The separation method of claim 58 further including the step of separating the elastic channel material from the optical mapping surface after adsorption of the polymeric molecule to the optical mapping surface.

60. The separation method of claim 57 further including the step of reacting the adsorbed polymeric molecule with a reactant.

61. The separation method of claim 60 wherein the reactant is an enzyme causing cleavage of the polymeric molecule.

62. The separation method of claim 60 wherein the reactant is a second polymeric molecule reacting with at least one elongated polymeric molecule.

63. The separation method of claim 57 wherein the polymeric molecules are DNA.

64. The separation method of claim 48 wherein the micro-channel includes a transparent wall and including the step of optically analyzing the sorted polymeric molecule suspended within the laminar flow.

65. The separation method of claim 48 further including the step of controlling the flow of liquid to cause elongation only of the polymeric molecules of a predetermined molecular weight range within the laminar flow.

66. The separation method of claim 65 further including the step of fixing the elongated polymeric molecules to a substrate.

67. The separation method of claim 65 further including the step of controlling the flow of liquid to separate the elongated and unelongated molecules as a function of their differing speed within the laminar flow and to separate the elongated molecules from the unelongated molecules by their different speeds in the laminar flow.

68. The separation method of claim 65 further including the step of obtaining a digital image of the elongated and unelongated molecules and separating them by image processing.

69. The elongation method of claim 48 wherein the micro-channel has a cross-sectional dimension within one order of magnitude of a relaxed diameter of the polymeric molecule.

70. The separation method of claim 48 further including the step of controlling the flow of liquid to separate the molecules as a function of their propensity to be adsorbed as a function of their length while moving in the laminar flow.

71. An apparatus for elongating a polymeric molecule comprising:
(a) an optical mapping surface;
(b) an elastic channel material releasably adhered to the optical mapping surface to create the micro-channel between the elastic channel material and the optical mapping surface sized to provide flow of a liquid and the polymeric molecule along a micro-channel length.

72. The apparatus of claim 71 wherein a cross sectional width of the micro-channel is substantially within one order of magnitude of the size of a relaxed dimension of a polymeric molecule to be processed.

73. The apparatus of claim 71 wherein the first wall of the micro-channel is transparent.

74. The apparatus of claim 71 wherein the first wall of the micro-channel is glass.

75. The apparatus of claim 71 wherein the first wall is treated to have a positive surface charge of predetermined density.

76. The apparatus of claim 71 including further at least one second wall of the micro-channel provides less electrostatic attraction to the polymeric molecule than the first wall.

77. The apparatus of claim 71 wherein the micro-channel is formed at least in part from poly(dimethylsiloxane).

78. The apparatus of claim 71 wherein the micro-channel size and a rate of flow of the liquid and polymeric molecule is selected so that diffusion of the polymeric molecule dominates sedimentation of the polymeric molecule.

79. The apparatus of claim 71 wherein a width of the micro-channels is between 1 and .01 times the straightened length of the polymeric molecule.

80. The apparatus of claim 71 wherein a width of the micro-channel is less than the diffusion distance of an end of the polymeric molecule during a passage time through the micro-channel.

81. The apparatus of claim 71 wherein a width of the micro-channel is less than 100 micrometers.

82. The apparatus of claim 71 wherein at least one end of the micro-channel provides a funnel section opening to a reservoir holding the liquid and polymeric molecules.

83. The apparatus of claim 71 wherein the means for passing the liquid and polymeric molecule through the micro-channel is a positive pressure pump attached at one end of the micro-channel.

84. The apparatus of claim 71 wherein the means for passing the liquid and polymeric molecule through the micro-channel is a negative pressure pump attached at one end of the micro-channel.

85. The apparatus of claim 71 wherein the means for passing the liquid and polymeric molecule through the micro-channel is a reservoir acted on by a force resulting from centrifugal acceleration.

86. The apparatus of claim 85 wherein the reservoir is at least one end well extending perpendicular to the length of the micro-channel and wherein the apparatus further includes a housing allowing the end well and micro-channel to be received by a centrifuge with the end well extending along a principal axis of centrifugal acceleration and the micro-channel extending substantially across the principal axis of centrifugal acceleration.

87. The apparatus of claim 71 wherein the polymeric molecule is DNA.

88. The apparatus of claim 71 wherein the micro-channel includes a region of varying cross section to promote a gradient in flow rate.

89. A method of manufacturing a micro-channel for straightening and fixing polymeric molecules, comprising the steps of;

- (a) preparing a mold of the micro-channels having a base plate and upstanding micro-channel cores;
- (b) coating the mold with an elastic molding compound;
- (c) removing the cured elastic molding compound from the mold; and
- (d) applying the cured elastic molding compound to an optical mapping surface to create micro-channels between the molding compound and the optical mapping surface.

90. The method of claim 89 including the step of treating the optical mapping surface to have a positive surface charge of predetermined density.

91. The method of claim 89 including the step of wherein the optical mapping surface is transparent.

92. The method of claim 89 including the step of wherein the optical mapping surface is glass.

93. The method of claim 89 including the step of wherein the elastic compound is poly(dimethylsiloxane).

94. An apparatus for manipulating polymeric molecules, the apparatus comprising:

a micro-channel sized to provide passage of a liquid along a micro-channel length; and

means for passing the liquid and polymeric molecule through the micro-channel to provide a laminar flow of varying flow rates increasing toward the center of the channel, the laminar flow operating to straighten the polymeric molecule by passage along the micro-channel within the laminar flow.